Abstracts

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Non-ST-Elevation Myocardial Infarction in Patients Undergoing Carotid Endarterectomy or Carotid Artery Stent Placement

Khan A, Adil MM, Qureshi AI, et al. Stroke 2014;45:595-7.

Conclusions: Non-ST-elevation myocardial infarction (NSTEMI) is not a benign event after carotid endarterectomy (CEA) or carotid artery stent (CAS) placement.

Summary: Most postoperative myocardial infarctions are NSTEMIs. The rates of periprocedural NSTEMI are not routinely measured after CEA or CAS. In this paper, the authors sought to evaluate the frequency of NSTEMI after CEA or CAS in overall clinical practice and determine relationships with in-hospital outcomes. NSTEMI frequency was determined using the Nationwide Inpatient Survey from 2002 to 2009. In-hospital outcomes assessed included mortality and composite of stroke, cardiac events, and mortality data. Of 1,083,688 patients who underwent CEA or CAS, 11,341 (1%) had documented NSTEMI during their hospitalization. With adjustment for constitutional variables and risk factors, NSTEMI was associated with higher rates of in-hospital mortality (odds ratio, 8.6; 95% confidence interval, 7.0-10.7; $P \leq .001$) and higher rates of the composite end point of stroke, cardiac events, and death (odds ratio, 14.6; 95% confidence interval, 13.0-16.5; $P \leq .0001$).

Comment: The findings demonstrate perioperative NSTEMI after CEA or CAS is infrequent. In fact, the rate seems lower than expected, likely reflecting the limitations of the database used for the study. However, it does appear that patients with NSTEMI after CEA or CAS may be more likely to have in-hospital adverse outcomes and therefore a significantly increased burden of health care resource use. These data do not indicate NSTEMI was the cause of the adverse outcomes after CEA or CAS but do suggest that it is a mark of more overall postoperative morbidity severity after CEA or CAS.

Observations from the IMPROVE trial concerning the clinical care of patients with ruptured abdominal aortic aneurysm

IMPROVE trial investigators. Br J Surg 2014;101:216-24.

Conclusions: Outcomes for repair of ruptured abdominal aortic aneurysms (rAAAs) might be improved by wider use of local anesthesia for endovascular aneurysm repair (EVAR) and by recognizing that a minimum blood pressure of 70 mm Hg may be too low a threshold for permissive hypotension.

Summary: Most data on outcomes of patients with rAAAs come from single-center studies and, as such, may be too small to identify clinical factors that could improve overall patient outcomes. The IMPROVE study, a pragmatic multicenter randomized clinical trial, allocated eligible patients with a clinical diagnosis of rAAA to a strategy of endovascular repair of rAAA (EVAR) or to open repair. IMPROVE showed no difference in 30-day mortality with a strategy incorporating EVAR for rAAA repair compared with a strategy of open repair for rAAA (IMPROVE trial investigators, Br Med J 2014;348:f7661). In this paper, the IMPROVE investigators sought to analyze influences of time and manner of hospital presentation, fluid volume status, type of anesthesia, type of EVAR, and time to aneurysm repair on 30-day mortality for rAAA. This was a prespecified plan of analyses to include only the patients who underwent aneurysm repair for a proven diagnosis of rAAA. Adjustments were made for potential confounding factors. In IMPROVE, 568 of 613 randomized patients had a symptomatic or rAAA, and diagnostic accuracy was 91%. Patients randomized outside routine working hours had higher operative mortality (adjusted odds ratio, 1.47; 95% confidence interval, 1.00-2.17). There was no difference in mortality rates between those patients admitted directly to a trial center vs those transferred to a trial center from a referring institution. Lowest systolic blood pressure was strongly and independently associated with 30-day mortality (51% among those with systolic blood pressures <70 mm Hg). In addition, patients who received EVAR under local anesthesia alone had reduced 30-day mortality compared with those who had EVAR under general anesthesia (adjusted odds ratio, 0.27; 95% confidence interval, 0.10-0.70). In patients with confirmed rupture, the time from randomization to the operating suite was not associated with 30-day mortality ($P = .415$).

Comment: The data indicate that a blood pressure of 70 mm Hg may be too low for optimal results in a patient with rAAA and that permissive hypotensive levels should be above this. In addition, when EVAR is used to treat a rAAA, it may be best to do it, if possible, under local anesthesia. Finally, the fact that results for repair of rAAA are no worse for a patient who is transferred than for those with a primary presentation to a specialist center, along with the fact that patients undergoing off-hours repair do more poorly, suggests a skilled multidisciplinary vascular team, including specialist anesthesia services, is likely to provide the best results for repair of a rAAA in any individual region. Outcomes for patients with rAAA therefore may be best served by a policy of regionalization of care for such patients to specialized centers.

Early graft failure after infrainguinal arterial bypass

Soma G, Greenblatt DY, Nelson MT, et al. Surgery 2014;155:300-10.

Conclusions: Early graft failure (EGF) after infrainguinal arterial bypass occurs in ~5% of patients and is strongly associated with additional complications and mortality.

Summary: Operative revascularization remains an important management tool in the care of patients with advanced claudication or critical limb ischemia. Most studies previously investigating EGF after infrainguinal bypass have been single-institution studies. The authors point out that two previous studies of this complication using a multi-institutional database were derived from an era before endovascular intervention had become as prevalent as is now (Singh N et al, J Vasc Surg 2008;47:556-61; and Conte MS et al, J Vasc Surg 2006;43:742-51). In this study, the authors used data from the American College of Surgeons National Surgical Quality Improvement Program to determine the frequency of 30-day EGF after infrainguinal arterial bypass. Univariate and multivariate analyses were then used to evaluate risk factors of EGF and additional complications associated in patients with EGF. Of 23,468 patients who underwent infrainguinal arterial bypass, 1065 (4.5%) had EGF. Patients who had EGF were more likely to have a prolonged duration of stay (34.8% vs 12.0%, $P < .001$), greater rates of reoperation (82.1% vs 14.3%, $P < .001$), and increased 30-day mortality (5.1% vs 2.1%, $P < .001$). The rate of additional complications in patients who experienced EGF was 42% compared with 25.4% in those who did not have EGF ($P < .001$). EGF in multivariate analyses was associated with younger age, female sex, black race, obesity, thrombocytosis, increased international normalized ratio, femoral-to-tibial bypass, prosthetic grafts, and emergency operation. Patients who experience complications in addition to EGF were more likely to have complications after graft failure (69.5% vs 31.3%).

Comment: The authors found an association between EGF and additional postoperative complications and overall mortality. The study perhaps helps identify preoperatively patients at higher risk of EGF who may benefit from targeted interventions, such as postoperative anticoagulation, to improve outcomes.

Cost-effectiveness and cost-utility of endovascular versus open repair of ruptured abdominal aortic aneurysm in the Amsterdam Acute Aneurysm Trial

Kapma MR, Dijksman LM, Reimerink JJ, et al. Br J Surg 2014;101:208-15.

Conclusions: In treatment of ruptured abdominal aortic aneurysm (rAAA), the increased costs for endovascular aneurysm repair (EVAR) means that it is unaffordable based on current standards of societal willingness-to-pay for health gains.

Summary: In recent years, there has been increased interest in the use of endovascular techniques for treatment of rAAA. Individual case series have suggested improved mortality with EVAR for treatment of rAAA compared with open treatment for rAAA. Two prospective trials, however, have concluded there is no difference in the efficacy of treatment. Additional possible drawbacks of EVAR are the high costs of the stent grafts and decreased applicability owing to anatomic insuitability of the AAA. The Amsterdam Acute Aneurysm trial was a multicenter trial in Amsterdam comparing open repair with EVAR in patients with rAAA (Reimerink JJ et al, Ann Surg 2013;258:248-56). This trial took place in two university academic medical centers and demonstrated equivalency of the end points of rates of death and severe complication in the patients treated with

EVAR and open repair. In the current study, the authors sought to analyze the cost-effectiveness and cost-utility of EVAR compared with a standard open repair in the treatment of rAAA, with costs per 30-day and 6-month survival as outcome parameters. Resource use was determined from the Amsterdam Acute Aneurysm trial data. Analysis was performed from a provider perspective. All costs were calculated as if patients had been treated in the same teaching hospital (Onze Lieve Vrouwe Gasthuis). The study randomized 116 patients. The 30-day mortality was 21% after EVAR and 25% after open repair, for an absolute risk reduction of 4.4% (95% confidence interval [CI], −11.0% to 19.7%). At 6 months, the total mortality rate for EVAR was 28% compared with 31% for those assigned to open repair (absolute risk reduction, 2.4%; 95% CI, −14.2% to 19.0%). The mean cost difference between EVAR and OR was 5306 (95% CI, − 1854 to 12,659) at 30 days and 10,189 (95% CI, − 2477 to 24,506) at 6 months. The incremental cost-effectiveness ratio per prevented death was 120,591 at 30 days and 424,542 at 6 months. There was no significant difference in quality of life between EVAR and OR. EVAR was not superior regarding cost-utility, either. In this study, the mean costs of the EVAR group were substantially raised by eight patients who required conversion to open repair. At 6 months, the mean difference between the converted and nonconverted groups was 19,981. The total costs required to save one person's life with EVAR was 120,446. At 6 months, this leads to a number needed to treat of 41.7 patients at 424,881 per life saved.

Comment: Overall, the Amsterdam Ruptured Aneurysm Study has indicated that EVAR for treatment of rAAA is associated with a slightly lower mortality rate but a considerably higher cost. The paper raises the interesting point: At what point are advances in medical technology affordable, and at what point do they become cost-prohibitive?

Effect of the first federally funded US antismoking national media campaign

McAfee T, Davis KC, Alexander RL Jr, et al. Lancet 2013;382:2003-11.

Conclusions: A high-exposure media campaign can be effective in increasing population-level quit attempts from smoking. The Tips media campaign could have added from a third to almost half a million quality-adjusted life-years to the United States (US) population.

Summary: Smoking kills >5 million people globally each year, including 440,000 people in the US alone. The US Centers for Disease Control and Prevention delivered a national, 3-month antismoking campaign called Tips From Former Smokers (Tips) that started in March 2012, in which hard-hitting, emotionally evocative television advertising was featured, depicting smoking-related suffering in real people. In this paper, the authors access the effects of the Tips media campaign. The authors performed baseline and follow-up surveys of nationally representative cohorts of adult smokers and nonsmokers. The national effect of the Tips campaign was estimated by applying rates of change in the cohort before and after the campaign to US census data. In the study, 3051 smokers and 2220 nonsmokers completed baseline and follow-up assessments. Of these, 2395 smokers (78%) and 1632 nonsmokers (74%) recalled seeing at least one Tips advertisement on television during the 3-month campaign. Quit attempts among smokers rose from 31.1% (95% confidence interval [CI], 30.3%-31.9%) at baseline to 34.8% (95% CI, 34.0%-35.7%) at follow-up, a 12% relative increase. The prevalence of abstinence at follow-up among smokers who made a quit attempt was 13.4% (95% CI, 9.7%-17.2%). Nationally, an estimated 1.64 million additional smokers made a quit attempt, and 220,000 (95% CI, 159,000-282,000) remained abstinent at follow-up. Recommendations by nonsmokers to quit grew from 2.6% at baseline to 5.1% at follow-up, and the prevalence of people talking with friends and family about the dangers of smoking rose from 31.9% (95% CI, 31.3%-32.5%) to 35.2% (95% CI, 34.6%-35.9%), resulting in an estimated 4.7 million additional nonsmokers recommending cessation services and >6 million talking about the dangers of smoking.

Comment: The Tips media campaign was a $54 million initiative that featured true emotional stories by former smokers to increase awareness of the human suffering caused by smoking and to encourage quitting and motivate nonsmokers to communicate with family and friends about the dangers of smoking. The campaign started on March 19, 2012, and was completed on June 10, 2012. Overall, enough Tips advertisements were broadcast for about four of five smokers to see at least one message. About one-third of television advertisements were tagged with 1-800-QUIT-NOW linking viewers to their state telephone help line, and about two-thirds carried a link to www.smokefree.gov, the National Cancer Institute's quit assistance Web site. The study demonstrates that immediate, measurable successful effects can be associated with a high-intensity public health campaign. Focused antismoking media campaigns can be another weapon in the arsenal to end the tobacco epidemic and potentially save millions of premature deaths and decrease worldwide health care costs. Additional campaigns in the US and internationally seem both medically and economically justified.

Comparison of Pregabalin with Pramipexole for Restless Legs Syndrome

Allen RP, Chen C, Garcia-Borreguero D, et al. N Engl J Med 2014;370:621-31.

Conclusions: Pregabalin significantly improves treatment outcomes of restless legs syndrome (RLS) compared with placebo, and augmentation rates are significantly lower with pregabalin than with 0.5 mg pramipexole.

Summary: RLS, also known as Willis-Ekbom disease, is a predominately nocturnal, rest-induced, distressing urge to move the legs. Anecdotally, it seems to occur in a number of patients with peripheral vascular disease, and clinically significant RLS effects ~2% to 3% of the European and American populations (Allen RP et al, Sleep Med 2010;11:31-7). Short-acting dopamine antagonists (pramipexole and ropinirole) and levodopa (Montplaisir J et al, Neurology 1999;52:938-43 and Mov Disord 2006;21:1627-35) have both been used for treatment. In this study, the authors sought to address questions about the efficacy of an alternative drug type in patients with RLS and about the iatrogenic nature of RLS augmentation. This was a 1-year blinded evaluation of efficacy and augmentation. Comparison was made between a dopaminergic drug pramipexole, administered at doses approved by the Food and Drug Administration for the treatment of RLS, with a nondopaminergic drug (pregabalin), an α2δ ligand with analgesic and anticonvulsant activity, also recently shown effective for treatment of RLS. This was a randomized, double-blind trial. Patients were randomly assigned to receive 52 weeks of treatment with pregabalin at a dose of 300 mg/d or pramipexole at a dose of 0.25 mg or 0.5 mg/d, or 12 weeks of placebo followed by 40 weeks of randomly assigned active treatment. The primary analyses involved a comparison of pregabalin and placebo over a 12-week period with the use of the International RLS Study Group Rating Scale, in which scores range from 0 to 40, with a higher score indicating more severe symptoms. The Clinical Global Impression of Improvement scale was also used to assess the proportion of patients with symptoms that were "very much improved" or "much improved." There was also comparison of RLS augmentation with pregabalin and pramipexole over a period of 40 or 52 weeks of treatment. A total of 719 participants received daily treatment, 182 with 300 mg pregabalin, 178 with 0.25 mg pramipexole, 180 with 0.5 mg pramipexole, and 179 with placebo. Over 12 weeks, the improvement (reduction) in mean scores on the International RLS scale was greater by 4.5 points among participants receiving pregabalin than among those receiving placebo ($P < .001$), and the proportion of patients with symptoms that were very much improved or much improved was also greater with pregabalin than with placebo (71.4% vs 46.8%, $P < .001$). The rate of augmentation over a period of 40 or 52 weeks was significantly lower with pregabalin than with pramipexole at a dose of 0.5 mg (2.1% vs 7.7%, $P = .001$) but not at a dose of 0.25 mg (2.1% vs 5.3%, $P = .08$). There were six cases of suicidal ideation in the group receiving pregabalin, three in the group receiving 0.25 mg pramipexole, and two in the group receiving 0.5 mg pramipexole.

Comment: RLS is an irritating disorder affecting many elderly patients, including those with peripheral vascular disease. The authors' data suggest that pregabalin is an effective treatment for the disorder and that worsening of the disorder can be due to an iatrogenic problem resulting from dopaminergic medications. One would hope that the days of treatment of RLS with a nocturnal dose of a mild sedative are over.

Prevalence of extracranial venous narrowing on catheter venography in people with multiple sclerosis, their siblings, and unrelated healthy controls: a blinded, case-control study

Traboulsee AL, Knox KB, Machan L, et al. Lancet 2014;383:138-45.

Conclusions: Chronic cerebrospinal venous insufficiency is rare in both patients with multiple sclerosis and in healthy patients.

Summary: Multiple sclerosis affects >2 million people worldwide and is a leading cause of neurologic disability. In recent years, a vascular origin of multiple sclerosis has been proposed with the observation by Zamboni et al that multiple stenoses of the extracranial venous drainage system may be present in patients with multiple sclerosis. In the original paper, venous blockages were present in all 65 patients with multiple sclerosis examined. This study was with ultrasound and catheter venography (Zamboni P et al, J Neurol Neurosurg Psychiatry 2009;80:392-9). These combinations of blockages were not seen in healthy control participants who were studied by ultrasound imaging or in patients with other diseases who underwent catheter venography. It was therefore speculated that venous blockages have a central role in the pathogenesis of multiple sclerosis and that treatment with venoplasty may improve the course of the disease (Zamboni P et al, J Vasc Surg 2009;50:1348-58). Zamboni et al then performed an unblinded, uncontrolled interventional treatment using venoplasty in patients with multiple sclerosis and claimed improvements in disability and quality of life. However, independent research groups have not been able to reproduce the findings of Zamboni et al regarding the diagnosis of chronic cerebrospinal venous